Lack of association between cathepsin D genetic polymorphism and Alzheimer disease in a Spanish sample.

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Cathepsin D (catD) is an intracellular aspartyl protease that exhibits beta and gamma secretase-like activity to cleave amyloid precursor protein int beta amyloid peptide. The T-allele of a biallelic (alleles C and T) polymorphism in the exon 2 of the catD gene has been found to be associated with increased risk of Alzheimer disease (AD) in two independent German populations. Other groups have been unable to replicate this association in Caucasian American and Northern Ireland populations. Moreover, a small and no significant tendency for the T-alle to be protective for AD has been demonstrated in Caribbean Hispanics. A case control study utilizing a clinically well-defined group of 311 sporad AD patients and 346 control subjects was performed to test this associati in an ethnically homogeneous population from Spain. We did not observ any association between the T-allele of the catD gene and the disease. Furthermore, catD was not predictive of AD in an interactive fashion wh considering apolipoprotein E, age, or gender. Copyright 2001 Wiley-Liss Inc.

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ELSEVIER SCIENCE FULL-TEXT ARTICLE

The genetic association between Cathepsin D and Alzheimer's disease.

Crawford FC, Freeman MJ, Schinka J, Abdullah LI, Richards D, Sevush S, Duara R, Mullan MJ.

Roskamp Institute and the University of South Florida Memory Disorder Clinic, 3515 E. Fletcher Avenue, Tampa, FL 33613, USA.

The aspartyl protease Cathepsin D has previously been suggested to play role in the Alzheimer's disease (AD) process because of its ability to clea the beta-amyloid precursor protein and the possibility that it may be one the 'secretase' enzymes. A functional C-->T polymorphism in the Cathep D gene (CATD) has been reported to be associated with increased risk fc AD in Caucasian case-control studies; specifically, the T-carrying genotypes confer increased risk. We have examined this association in ou own Caucasian dataset of 210 AD cases and 120 controls, and in an additional Hispanic dataset comprising 79 AD cases and 112 controls. In Hispanics we find a modest interaction between CATD genotype and age of onset on risk for AD, such that the non-T-carrying genotype confers increased risk. In our Caucasian dataset we find no evidence for associati between the CATD polymorphism and AD, although we do observe a small tendency towards an increase in the T-carrying genotypes in the ca group, consistent with previous studies. We conducted an aggregate analysis of the published Caucasian datasets and found evidence that this CATD polymorphism (or another locus in linkage disequilibrium) does contribute significant, but small (<2%) risk for AD.

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Non-replication of association between cathepsin D genotyp and late onset Alzheimer disease.

Menzer G, Muller-Thomsen T, Meins W, Alberici A, Binetti G, Hocl C, Nitsch RM, Stoppe G, Reiss J, Finckh U.

Department of Human Genetics, University Hospital Hamburg-Eppendo Germany.

In two recent studies from Germany, a strong association was found between the allelic variant T of the amino acid substitution encoding polymorphism 224 C/T (A38V) in exon 2 of the cathepsin D gene (CTSI and late onset Alzheimer disease (AD). Other studies from Europe and th USA revealed ambiguous results. Therefore, we performed an independe association study on CTSD and AD in a sample of 324 Caucasian patient from Germany, Switzerland, and Italy with late onset AD, and 302 non-demented controls. We could not confirm an association between CTSD genotype and AD, although there was a slight but not significant increase in frequency of the T allele and T carrier status in AD. Post hoc data analyses suggested that there might be a stronger effect of CTSD genotype on AD risk in males, and an interaction between CTSD and APOE genotypes in males but not females.

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- Ann Neurol. 2000 Mar;47(3):399-403.

Cathepsin D polymorphism not associated with Alzheimer's disease in Japanese.

Matsui T, Morikawa Y, Tojo M, Okamura N, Maruyama M, Hirai F Chiba H, Matsushita S, Higuchi S, Arai H, Sasaki H.

Publication Types:
- Comment
- Letter

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